PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1132WOORD01		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/08967	13.08.2003	17.08.2002

International Patent Classification (IPC) or both national classification and IPC
C07D221/12

Applicant
ALTANA PHARMA AG

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.03.2004	20.04.2004

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/08967

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-36 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 12,13

   because:

   ☒ the said international application, or the said claims Nos. 12,13 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	

2. Citations and explanations

   see separate sheet

1) The present application relates to guanidinoyl substituted phenylphenanthridines having PDE3/4 inhibiting activity.

2) The following documents are cited:
D1: WO 99 05113 A
D2: WO 02 06238 A
D3: WO 97 28131 A
D4: EP-A-1 270 577
D5: EP-A-0 490 823
D6: WO 02 066476 A

Document D6 was published before the filing but after the priority date of the present application. The priority seems not valid for claim 1 and claims 7-13 in as far as dependend on claim 1. For these claims D6 is considered as prior art.

3) Novelty
Documents D1-D3 describe subsitutued phenylphenathridines, which are not guanidinoyl subsituted derivatives.
Document D4 mentiones a guanidinoyl-phenyl subsituted furo-isoquinoline (see compound 150) but no phenylphenathridines.
Document D5 desribes phenyl subsituted isoquinolines but no phenylphenathridines or guanidinoyl-phenyl subsituted derivatives.
The compounds of document D6 are not comprised in the definition of the compouds of the present application.

4) Inventive step
Documents D1-D3 may be considered as closest prior art describing related compounds with PDE3/4 inhibiting activity.
Merely as solution to the problem of providing alternative agents with PDE3/4 inhibiting activity, the claimed subject-matter would seem obvious.
From the variety of possible substitutions it would be evident to the person skilled in the art that the subsitutions to the phenyl group are very not critical for the activity of the compounds. The structural modification in the form of a guanidinoyl group instead of a substituted aminocarbonyl group would seem a minor modification, which in the light of the variety of substitutions in the prior art would not be likely to cancel ther relevant activity. In fact a (cyclic) guanidinoyl phenyl

group has been referred to in D4 in the context of structurally related PDE4 inhibitors.

This objection is further supported by D6 in as far as the priority is not valid as this document mentions the relevant guanidinoyl group in a related series of benzonaphthyridines.

5) Further observations
Claims 12 and 13 relate to a method of therapeutic treatment.